Mestrado em Educação para a Saúde

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Family and sociodemographic influences on the pain experience of 7-year-old children as reported by parents - a study of the Generation XXI birth cohort

Porto | 2016

Dissertação de candidatura ao grau de Mestre em Educação para a Saúde, apresentada à Faculdade de Medicina da Universidade do Porto e à Faculdade de Psicologia e Ciências da Educação da Universidade do Porto, realizada sob a orientação científica da Doutora Raquel Lucas Calado Ferreira - Instituto de Saúde Pública da Universidade do Porto; Departamento de Epidemiologia Clínica, Medicina Preditiva e Saúde Pública da Faculdade de Medicina da Universidade do Porto.

Ao abrigo do Art.º 8º do Decreto-Lei n.º 288/70 esta dissertação tem por base dois manuscritos, nos quais colaborei ativamente na definição das hipóteses, bem como na análise e interpretação dos dados. Fui também responsável pela redação da versão inicial dos dois manuscritos:

I. Gender shaping of the pediatric pain experience from age seven: parental report, psychosocial triggers and consequences

II. Socioeconomic context, living conditions and the pediatric pain experience: parental report of chronic widespread pain features in 7-year-old children

Agradecimentos

À Raquel, agradeço a paciência e excelente orientação que me proporcionou ao longo deste percurso. Agradeço também por ter conseguido sempre, no seu jeito prático e objetivo, "obrigar-me" a pensar de forma científica e levar-me pelos diversos caminhos possíveis em relação a este tema tão complexo. Sem dúvida que, apesar de ter realizado este percurso à distância, levo bastantes ensinamentos deste ano. O principal é a importância de colocar sempre o máximo em tudo que fazemos, nunca descorando o rigor e profissionalismo em cada documento ou tabela. E outro, também muito importante, o de levar a vida com sentido de humor e a sorrir. Todas as reuniões tinham sempre um toque de descontração e boa disposição. E assim dá bem mais gosto trabalhar.

À Ana Raquel Martins, agradeço a sua amabilidade e prontidão para me ajudar sempre que precisei. Agradeço ainda o facto de estar sempre disponível ao longo deste ano, fosse pessoalmente, por *email* ou via telemóvel. Apesar de ter passado pouco tempo na sala 406, sempre me senti "em casa", principalmente por te-la lá e pela sua preocupação em me ajudar a sentir bem e integrada. Muito obrigada por isso. Foste uma excelente colega.

À restante *Bone team:* Teresa, Fábio, Daniela, Ivo, Alexandra e Sara; tenho a agradecer todas as discussões e partilhas que tivemos ao longo das reuniões, bem como todos os contributos que deram para que esta tese se tornasse no que é hoje.

Aos restantes "residentes" da sala 406, agradeço a simpatia com que me receberam nas vezes em que me desloquei ao ISPUP e por lá fiquei a trabalhar.

Agora em relação aos de sempre. Agradeço aos meus amigos pela paciência ao longo deste ano. Agradeço ao Rui, Rute, Raquel e Renata pelo apoio e pela compreensão de todas as minhas recusas e ausências ao longo deste percurso. É difícil ter de abdicar da vida social e ter de renunciar a convites continuamente, mas vocês sempre compreenderam e me apoiaram neste percurso. E isso foi sem dúvida fundamental. Às minhas queridas amigas do trabalho, Marlene e Paula, que sempre me facilitaram a vida quando precisei de faltar e sair mais cedo. Além disso, tal como a Alice, ouviram-me vezes e vezes sem conta a falar sobre este assunto, lidaram com as minhas crises de

nervos e sempre me deram ânimo e força para continuar. À Bruna, à Mariana e à Gisela por, apesar da distância, estarem sempre presentes e nunca me deixarem cair. À Nídia pela sua enorme luz e força, que me inspira a querer ser sempre mais e melhor. Ao meu *personal trainer* e amigo, Rui, por ser um exemplo de ambição, foco na carreira e na melhoria das suas competências. Pessoas assim estimulam-me a crescer, quer a nível pessoal, quer a nível profissional.

Aos meus pais e irmão. Aos meus pais por sempre me estimularem a crescer a todos os níveis e por sempre me proporcionarem oportunidades de aprendizagem e desenvolvimento. Ao meu irmão, por ter um papel indispensável na minha vida e por saber que nunca estarei só enquanto ele existir.

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Resumo

Introdução

As diferenças entre géneros na experiência da dor estão bem estabelecidas em adultos, com as mulheres a reportar mais dor. Na infância estas diferenças na prevalência da dor normalmente já são aparentes e parecem determinar um percurso para a presença de dor crónica no futuro. Contudo, a maioria dos estudos de dor experimental em crianças apenas encontrou diferenças entre géneros, nas respostas à dor, quando a idade média era acima dos 12 anos. Esta evidência suporta que a experiência da dor crónica ao longo da vida tem especificidades de género que se tornam mais evidentes com o crescimento, devido ao desenvolvimento a nível sexual/hormonal e em relação aos papéis sociais de cada género. Além disso, os mecanismos que originam o comportamento da dor e sofrimento são moldados ao longo da vida. Este modelo teórico é consistente com observações empíricas de que uma experiência de dor prévia é o maior marcador de risco para um novo episódio de dor. Pensa-se que, ao longo da vida, os determinantes da experiência da dor atuem em diferentes níveis, desde influências individuais até contextuais, desde o contexto psicossocial às características sociodemográficas.

Objetivos

Objetivo I: Verificar se as diferenças entre géneros na experiência da dor já são observáveis em crianças com sete anos de idade, especificamente em relação ao reporte dos pais, aos *triggers* psicossociais e à severidade das consequências.

Objetivo II: Verificar se o contexto psicossocial, aos sete anos, prediz as características de dor pediátrica que se assemelham à síndrome de dor crónica generalizada.

Métodos

Objetivo I:

Usamos dados de 5834 crianças de 7 anos de idade da coorte Geração XXI (2840 raparigas (48.7%) e 2994 rapazes (51.3%)). A dor foi avaliada através da versão portuguesa do *Luebeck Pain Screening Questionaire*. As frequências absolutas e relativas foram estratificadas por género da criança e do respondente. A significância estatística das diferenças entre grupos foi avaliada através do teste Qui-quadrado. Os dados foram analisados usando SPSS 22.0 e Stata 11.2.

Objetivo II

Usamos dados de 5834 crianças de 7 anos de idade da coorte Geração XXI. A dor foi avaliada através da versão portuguesa do *Luebeck Pain Screening Questionaire*. As características individuais foram recolhidas através de questionários aplicados em entrevistas individuais. A significância estatística das diferenças nas proporções entre grupos foi usada através do teste qui-quadrado. Para estimar as associações das variáveis individuais e contextuais com os três *outcomes* do estudo, recorreu-se à regressão logística, comparando: 1) crianças com queixas de dor nos últimos três meses versus as restantes; 2) crianças que identificaram eventos psicossociais como causas da dor versus as restantes; 3) crianças com dor em mais do que uma localização versus as restantes.

Resultados

Objetivo I

As raparigas foram reportadas como experienciando dor mais frequentemente que os rapazes (46.7% vs 42.9%, p=0.004). Das crianças com dor, a severidade era,

geralmente, reportada como mais elevada nas meninas, exceto na intensidade da dor. Relativamente ao respondente, nas raparigas, todas as características eram estatisticamente diferentes entre respondentes: quando comparadas com os pais, as mães mais frequentemente reportaram qualquer dor (47.4 vs. 31.2%, p=0.002) e todas a características da dor analisadas. Nos rapazes, a única diferença estatisticamente significativa entre mães e pais respondentes era em relação à presença de dor (43.3 mães vs. 33.3% pais, p= 0.037). O reporte dos pais não diferiu entre género da criança, no entanto, as mães reportaram piores características da dor para as raparigas.

Objetivo II

Circunstâncias psicossociais para o início da dor foram identificadas por 16.9% dos pais. Todas as características apresentaram diferenças estatisticamente significativas entre géneros: com os pais das meninas a reportarem pior padrão de dor. As variáveis sociodemográficas não estavam estatisticamente associadas com a dor de qualquer género. O reporte recente de dor também não estava associado aos indicadores de suporto social, em nenhum dos géneros. No entanto, os indicadores das condições de vida mostraram um gradiente social, em ambos os géneros, em relação às características da dor: meninas e meninos que não tinham jardim em casa tinham maior propensão para se reportarem de dor de início psicossocial (meninas: OR= 1.380, 95% CI: 1.137, 1.674; meninos: OR= 1.220, 95% CI: 0.994, 1.498). As meninas cujas famílias não contratavam empregada doméstica tinham mais tendência a reportar dor de início psicossocial (OR= 1.364, 95% CI: 1.039, 1.791). Os rapazes e raparigas cujos pais reportaram humidade ou bolor em casa tinham mais propensão para reportarem todos os *outcomes* em estudo: presença de dor (meninas: OR= 1.246, 95% CI: 1.054, 1.474; meninos: OR= 1.332, 95% CI: 1.132, 1.569), dor em mais do que uma localização (meninas: OR= 1.306, 95% CI: 1.097, 1.556; meninos: OR= 1.362, 95% CI: 1.103, 1.681) e dor de início psicossocial (meninas: OR= 1.267, 95% CI: 1.030, 1.560; meninos: OR= 1.308, 95% CI: 1.052, 1.627).

Conclusões

A nossa investigação mostrou uma interação entre os géneros dos pais e dos respectivos filhos no reporte da experiência de dor, que já é evidente aos sete anos de idade. Além disso, o início psicossocial era independente do género quando se determinava o impacto negativo que tinha no quotidiano das crianças e nas atividades de socialização. Por último, aos sete anos, as condições da casa desfavoráveis estavam associados com o reporte parental de dor em mais do que uma localização e com o início psicossocial. Estas pareciam ser independentes dos indicadores sociodemográficos clássicos e do suporte social, sugerindo que esta pode ser uma fase crucial para prevenir a influência sociodemográfica no padrão de dor.

Abstract

Introduction

Gender differences in pain are well established in adulthood, with women reporting more pain. In childhood these differences in pain prevalence are generally already apparent and seem to set a life course determination for chronic pain. However, the majority of studies of experimental pain tasks in children only found differences between genders in pain-related responses, when mean age was above 12 years old. This body of evidence supports that the life course experience of chronic pain has gender specificities that become more evident with growth, as both sexual dimorphism and gender roles develop and accentuate. Moreover, the mechanisms that originate pain behavior and suffering are shaped throughout the life course. This theoretical model is consistent with empirical observations that prior pain experience is the main risk marker for a new episode of pain. Throughout the life course, the determinants of pain experience are thought to act at different, nested levels, from individual to contextual influences, ranging from psychosocial context to sociodemographic characteristics.

Objectives

Objective I: To assess whether gender differences are already observable in the pain experience of seven-year-old children, specifically regarding parental report, perceived psychosocial triggers and severity of consequences.

Objective II: To assess whether psychosocial context predicts features of pediatric pain that overlap the chronic widespread pain syndrome from as early as age seven.

Methods

Objective I:

We used data from 5834 seven year old children from Generation XXI cohort (2840 girls (48.7%) and 2994 boys (51.3%)). Pain was assessed using the Portuguese version of Luebeck Pain Screening Questionaire. Absolute and relative frequencies were stratified by gender of the child and of the respondent. The statistical significance of differences between groups was assessed using Pearson's chi-squared test. Data were analyzed using the SPSS 22.0 and Stata 11.2.

Objective II

We used data from 5834 seven year old children from Generation XXI cohort. Pain was assessed using the Portuguese version of Luebeck Pain Screening Questionaire. Individual characteristics were assessed through questionnaires applied in individual interviews. The statistical significance of differences in proportions between groups was assessed using Pearson's chi-squared test. To estimate the associations of contextual and individual variables with three study outcomes, logistic regression was conducted, comparing: 1) children with pain complaints in the preceding three months versus the remaining children; 2) children with psychosocial events for the onset of pain versus all the remaining children, and 3) children with multisite pain versus all the remaining children.

Results

Objective I

Girls were reported to have experienced any pain more frequently than boys (46.7% vs 42.9%, p=0.004). Among children with pain, severity was generally reported as higher in girls for all features except pain intensity. According to the caregiver who responded to the questionnaire, in girls, all features were significantly different between

respondents: when compared to fathers, mothers more frequently reported any pain (47.4 vs. 31.2%, p=0.002) and all analyzed pain features. In boys, the only significant difference between mother and father respondents was regarding pain presence (43.3 mothers vs. 33.3% fathers, p= 0.037). Paternal report did not differ between genders of the child but mothers reported worse symptoms for girls than for boys.

Objective II

Psychosocial circumstances at the onset of pain were identified by 16.9% of parents. All characteristics showed significant differences by gender: with girls' caregivers reporting worse pattern of pain. Sociodemographic background variables were not significantly associated with pain in either gender. Recent pain report was not associated with social support indicators, in either gender. However, indicators of living conditions showed a social gradient in both genders with regard to different pain outcomes: girls and boys who did not have a garden at home were significantly more likely to be reported to complain of pain of psychosocial onset (girls: OR= 1.380, 95% CI: 1.137, 1.674; boys: OR= 1.220, 95% CI: 0.994, 1.498). Girls whose family did not hire a housekeeper had higher odds of pain of psychosocial onset (OR= 1.364, 95% CI: 1.039, 1.791). Both boys and girls whose parents reported dampness or mold at home were more likely to report all pain outcomes: any pain (girls: OR= 1.246, 95% CI: 1.054, 1.474; boys: OR= 1.332, 95% CI: 1.132, 1.569), multisite pain (girls: OR= 1.306, 95% CI: 1.097, 1.556; boys: OR= 1.362, 95% CI: 1.103, 1.681) and pain of psychosocial onset (girls: OR= 1.267, 95% CI: 1.030, 1.560; boys: OR= 1.308, 95% CI: 1.052, 1.627).

Conclusions

Our investigation showed an interaction between parental and offspring genders on the report of the pain experience, which was already evident at age seven. Nevertheless, a recognized psychosocial onset was independent of gender in determining the negative impact of pain on the child's daily living and socialization activities. Also, at seven years of age, poor living conditions were associated with parental report of multisite

pain and pain of psychosocial onset. These seemed to be independent of classic indicators of deprivation and social support, suggesting that this might be a key stage in life to prevent an adverse socioeconomic patterning of the pain experience.

Introduction

Chronic pain is an enormous public health problem, with 10% of the world's population being diagnosed with new cases each year [1] and, with a prevalence, in the previous 12 months, of 37% in developed countries [2]. Chronic pain is also a problem in childhood and adolescence, with rates increasing as age increases [3]. This problem can affect all countries and populations, independently of age, ethnicity, income or geography. However, it is not equally distributed across the world, with pain characteristics (intensity, duration, frequency) varying in a wide range [1].

Frequently, pain is not limited to one site; it is associated with other sites and unpleasant sensory and emotional experiences which can lead to dysfunctional cognitions and behaviors [4]. When regional pain becomes chronic and spreads to several anatomical sites, it becomes known as chronic widespread pain (CWP) [5-7] which is an important measure of the global burden of pain. CWP is even more disabling than regional pain, with a reported population prevalence of 2% to 18% [7, 8]. CWP is defined as pain in both sides of the body and above and below the waist, plus pain in the axial skeleton [9].

Chronic pain has great impact on people's lives causing inability to work, concomitant illness (anxiety, depression, and suicidal thoughts), disrupted social relationships and frequent use of healthcare [1]. Moreover, multisite pain is associated with increased risk of functional problems [10]. Even in adolescents and children, it is described that their quality of life is negatively influenced because of sleep problems, inability to pursue hobbies and also disrupted social life [11]. This means that chronic pain has a deep impact on individuals and the society in general.

Determinants of pain

Research has found the following main risk factors for chronic pain: female gender, older age, lower socioeconomic status, occupational factors and history of abuse and interpersonal violence [12, 13]. However, the most important risk marker is a prior episode of pain, and in a prospective study which studied risk factors for widespread pain onset, the most important predictor was the number of pain sites at baseline [14].

Prospective population study reported that the number of pain sites was stable over 7 years, which suggest that pain may persist or recur once established [15]. This shows that individuals with multisite pain are at increased risk of developing chronic widespread pain and deserve further attention.

The leading theory, nowadays, for the development of chronic pain is a bio-psycho-social model [16], in which biological, psychological [17], social [16] and behavioral factors have been identified has playing a role in the transition to chronic pain [18, 19]. Although research is not completely consistent regarding psychological factors, there is evidence that fear, anxiety and catastrophizing influence pain perception and behavior [20, 21]. Henningsen et al (2003) [22], in a systematic review, showed an association between unexplained physical symptoms and depression and anxiety. Using population based data from 17 countries, Gureje et al (2008) [23] found that an increasing number of pain problems is accompanied by an increase in the prevalence of depressive illness, and various anxiety disorders. Similarly, psychological factors were strongly associated with the likelihood of symptom persistence in all types of regional pain syndromes, in contrast with mechanical factors (such as workload) which were only associated with each specific regional pain syndrome [24]. This highlights the relationship between psychosocial contexts and pain and the need to further study these individuals. In terms of socioeconomic factors, Jordan et al (2008) [25] found that perceived income inequalities, lower educational level and neighborhood deprivation were related with the onset of disabling pain, although less evident than age, anxiety or depression and multisite pain. The results of Smith et al. 2001 [26] regarding chronic pain were similar.

Transgenerational experience of pain is also a key influence, as shown by birth cohort studies that found that children with parents with chronic pain are more likely to develop that problem [27, 28], maybe due to the fact that sensitivity to painful stimuli and pain tolerability is, to a large extent, determined by our genes [29, 30] as well as by the shared psychological and social environment related to the family [31].

Pain as a life course experience

The majority chronic pain cases do not start in adulthood, with the first episode of pain being placed in adolescence or even childhood. There is evidence showing that children reporting pain are more prone to report pain in adulthood. A 25-year prospective study found that 14 year old children who reported low back pain in the recruitment phase were significantly more likely to report more low back pain and with worse consequences in adulthood [32]. Also, the report of widespread pain was highly predictive of the same pattern during follow-up, which suggests that the pain pathway may begin at an early age and continue through adulthood [33, 34]. This is also consistent with studies that show frequent multisite complaints among school children [35-37].

Another interesting finding is that childhood adversities (sexual or physical abuse, neglect, parental death or separation) seem to modulate the development of chronic pain conditions in the future [38, 39]. Women with fibromyalgia are more likely to have been victims of rape and sexual or physical abuse in childhood [40-42]. The study of Sansone et al (2010) [43] found that being bullied in childhood was associated with higher pain rating in adulthood. Scharff (2005) [44] showed that pain-related disability among children was associated to high levels of family conflict. Birth factors (low birth weight and neonatal intensive care admission) and memories of childhood experiences of pain or illness are also associated with recurrent pain status in adulthood, which may be related to learned behavior and modeling that are considerably potent in childhood [45]. In childhood, poor social interactions and adverse lifestyles are associated with pediatric pain. Taken together, these findings suggest that "pain experience in childhood is an important predictor of (chronic) pain in adulthood" [42], supporting the theory of pain as a life course experience.

Differences between genders

As written before, being a woman is a risk factor for pain. Women report pain with higher frequency, longer persistence and greater intensity than men. They also report a higher number of pain sites and greater resulting disability [46].

The causes of these phenomena remain unclear. There is uncertainty about whether they are due to biological factors or psychosocial and cultural influences – or to an interaction between all of these - and about whether there are critical development periods for their influences during the life course [46]. Unruh (1996) [47] stated some important areas for research in this field. In this thesis, we focused on two: (1) exploration of the extent to which gender is associated with fundamental features of pain (frequency, duration, and severity); and in a less extended level (2) understanding the relationship between gender, age, and pain experience, since we studied a specific young age not yet very "polluted" regarding hormonal changes and sociodemographic impact.

Some theories exist that relate to: 1) exposure, where women are more exposed to risk factors than men; 2) gender roles, which assume that it is more acceptable for women to express pain; and 3) vulnerability, according to which women are more biologically predisposed to develop pain than men [3]. However it is not clear how the models might interact with each other.

Methodological challenges studying pain

Pain is a subjective experience. This is a terrible methodological issue because there is no objective way to measure it. It depends on the individual perception, which is related to individual, social and cultural factors. Another problem is that there is a wide range of instruments to measure it and, in the specific case of chronic pain, definitions vary across studies, which makes it very difficult to compare frequencies and come to clear conclusions on the burden of pain.

Also, there is a wide range of pain characteristics. Some studies focus on pain location, others on its duration and others on specific syndromes such as chronic widespread pain. Moreover, pediatric pain is especially challenging since it comprises subjects from age 0 to 18 years where individual biological, psychological and even social circumstances change dramatically. However, the majority of studies is based on small samples and includes wide age ranges. This also makes it difficult to assess the features and implication of pain at each specific age. Also, many pain problems emerge early in

life, so it is quite difficult to study the onset of the first episodes of pain without targeting very young children.

Another problem is the recall period. Some studies ask for the presence of pain in the last month, whilst others ask for the pain experience in the last year. This is a problem because individuals may have experienced pain but at the time of questioning they may not recall it. On the other hand, it can be assumed that if a subject does not recall a pain episode it was not important in their perception so it is not object of study. This would imply that the pain that matters most for research is the pain that is recalled over time.

Finally, studying pain and its determinants through a cross-sectional design can be subject to important reverse causation, in that pain experience itself may have an influence on the determinants under study, namely in the psychological sphere.

This thesis is important because…

Chronic pain is a major problem in adulthood, with high burden for individuals and society. It is known that pain also affects children and adolescents. Moreover, the first episode of pain frequently occurs early in life and persists or recurs into adulthood. Given this, it is difficult to assess pain onset because most studies are in adult populations or in adolescents. So, firstly this thesis responds to this need. It is a large population based study with children of young age, i.e. 7 years old.

Gender differences in the prevalence of pain are well established in adults. However, differences in pain features and consequences deserve further attention, mainly in pediatric samples. It remains unclear when or why these differences start to be significant. Some explanations rely on biological factors such as different hormonal environment after puberty. This thesis gives another perspective of this issue because it studies a sample where major puberty changes have not yet occurred and differences in pain prevalence and characteristics are less likely to have biological grounds.

Also, psychosocial factors and multisite pain are markedly associated with the onset of chronic widespread pain. This is a syndrome that deserves attention because its burden

and prognosis is even worse than that of chronic pain. Since pain is a life course experience, in this thesis, we assessed children whose parents report those specific characteristics (psychosocial factors and multisite pain), considering them at risk of developing chronic widespread pain in the future, and looked for determinants (biological, sociodemographic and lifestyle) that could suggest leverage points for prevention.

The Generation XXI cohort

Generation XXI is the first Portuguese birth cohort. Participants were recruited, between April 2005 and August 2006, in the five public maternity units of Porto metropolitan area. The main objectives were to study maternal and infant health indicators and to understand the relation between progenitor's characteristics and the development of the children in the first years of life in order to study risk markers for future health conditions.

Participants

During the recruitment period, all women who delivered a live-born (gestational age > 24 weeks) were invited to participate in this cohort. A total of 91.4% of mothers accepted to participate, making a total of 8495 mothers and 8647 infants. The first follow-up of the whole sample was at age 4. In this evaluation 5977 (69.1% of the initial sample) children were assessed. The second follow-up wave was at age 7 and took place between April 2012 and April 2014, where 5843 children were evaluated (67.6% of the initial sample). The third follow up (at 10 years old) has started in August 2015 and is expected to be concluded in December 2016.

The Generation XXI study protocol was approved by the University of Porto Medical School/ S. João Hospital Centre ethics committee and by the National Committee for Data Protection. All procedures were followed according to the Declaration of Helsinki.

Data collection

To this thesis, only children present to the age 7 follow-up were included. This evaluation wave had as main objectives, namely to evaluate: 1) growth, nutrition and body composition; 2) use of health care services; 3) relevant socioeconomic aspects to childhood development; and 4) children health status. In order to answer these objectives, information was collected by trained health professionals using structured questionnaires and an extensive physical examination. The procedures of this evaluation took place at the Department of Clinical Epidemiology, Predictive Medicine and Public Health in Medical School of the University of Porto and included:

- Questionnaires: parents or other caregivers responded to a structured questionnaire mainly focused on the child and the surrounding context, physical activity, food frequency, sleeping habits and **pain** (Portuguese version of the Luebeck Pain-Screening Questionaire). Other specific questionnaires were also applied to the children but were not object of study in this thesis.
- Physical Examination;
- Blood samples;
- Dental evaluation;
- Musculoskeletal Evaluation: Standing and sitting posture was assessed.

Aims

By using cross-sectional data from the seven year-old evaluation of the Generation XXI population-based birth cohort the objectives were:

1. To assess whether gender differences are already observable in the pain experience of seven-year-old children, specifically regarding parental report, perceived psychosocial triggers and severity of consequences (Chapter I);

2. To assess whether psychosocial context predicts features of pediatric pain that overlap the chronic widespread pain syndrome from as early as age seven (Chapter II);

Descriptive results

Socioeconomic characteristics and gender of the respondent

Table 1. Distribution and associations (chi-square test) between indicators of socioeconomic position and gender of the respondents: mothers or fathers

	Child with mother report (n= 5513)	**Child with father report (n= 207)**		
	n (%)	**n (%)**	**p**	**X^2**
Sociodemographic background				
Child gender				
Feminine	2686 (48.7)	96 (46.4)	0.508	0.439
Masculine	2827 (51.3)	111 (53.6)		
Parental marital status				
Together	4760 (86.4)	177 (85.5)	0.702	0.146
Separated	747 (13.6)	30 (14.5)		
Siblings				
No	2122 (38.5)	86 (41.5)	0.375	0.786
Yes	3391 (61.5)	121 (58.5)		
Caregiver education				
Basic	2215 (40.2)	77 (37.2)	0.348	2.112
Secondary	1657 (30.1)	72 (34.8)		
Higher	1639 (29.7)	58 (28.0)		
Monthly household income (Euro)				
≤ 1000	1576 (29.3)	50 (24.8)		
1001 – 2000	2528 (47.0)	100 (49.5)	0.529	2.217
2001 – 3000	938 (17.5)	37 (18.3)		
>3000 €	332 (6.2)	15 (7.4)		
Parental occupation				
Full-time	3789 (68.8)	139 (67.1)	0.286	2.506
Part-time	421 (7.6)	22 (10.6)		
Unpaid	1294 (23.5)	46 (22.2)		
Concern about household expenses				
Never or rarely	313 (5.7)	13 (6.3)	0.384	1.916
Sometimes or a lot of times	1200 (22.0)	53 (25.7)		
Almost always or always	3952 (72.3)	140 (68.0)		
Child's school type				
Private	524 (9.5)	20 (9.7)	0.939	0.006
Public	4963 (90.5)	186 (90.3)		
Garden				
No	3110 (56.5)	99 (47.8)	0.014	6.089
Yes	2395 (43.5)	108 (52.2)		
Housekeeper				
No	4514 (82.0)	165 (79.7)	0.395	0.724
Yes	989(18.9)	42 (20.3)		
Dampness or mold				
No	4053 (73.5)	136 (66.3)	0.019	5.514
Yes	1445 (26.3)	69 (33.7)		
Internet connection				
No	623 (11.3)	29 (14.0)	0.232	1.426
Yes	4880 (88.7)	178 (86.0)		
Holidays away				
No	1407 (25.5)	59 (28.5)	0.335	0.930
Yes	4106 (74.5)	148 (71.5)		

*Missings vary between 94 and 238 in the question about household income

In table 1, it is possible to observe that there are no significant statistical differences in classic socioeconomic variables regarding gender. The presence of dampness at home and having a garden were the only ones different between respondents, with fathers reporting more than mothers.

ChapterI

Gender shaping of the pediatric pain experience from age seven: parental report, psychosocial triggers and consequences

Abstract

Background: Gender differences in pain are well established in adulthood, with women reporting more pain. In childhood these differences in pain prevalence are generally already apparent and seem to set a life course determination for chronic pain. However, the majority of studies of experimental pain tasks in children only found differences between genders in pain-related responses, when mean age was above 12 years old. This body of evidence supports that the life course experience of chronic pain has gender specificities that become more evident with growth, as both sexual dimorphism and gender roles develop and accentuate.

Objective: To assess whether gender differences are already observable in the pain experience of seven-year-old children, specifically regarding parental report, perceived psychosocial triggers and severity of consequences.

Methods: We used data from 5834 seven year old children from Generation XXI cohort (2840 girls (48.7%) and 2994 boys (51.3%)). Pain was assessed using the Portuguese version of Luebeck Pain Screening Questionaire. Absolute and relative frequencies were stratified by gender of the child and of respondent. The statistical significance of differences between groups was assessed using Pearson's chi-squared test. Data were analyzed using the SPSS 22.0 and Stata 11.2.

Results: Girls were reported to have experienced any pain more frequently than boys (46.7% vs 42.9%, p=0.004). Among children with pain, severity was generally reported as higher in girls for all features except pain intensity. According to the caregiver who responded to the questionnaire, in girls, all features were significantly different between respondents: when compared to fathers, mothers more frequently reported any pain (47.4 vs. 31.2%, p=0.002) and all analyzed pain features. In boys, the only significant difference between mother and father respondents was regarding pain presence (43.3 mothers vs. 33.3% fathers, p= 0.037). Paternal report did not differ between genders of the child but mothers reported worse symptoms for girls than for boys.

Conclusion: Our investigation showed an interaction between parental and offspring genders on the report of the pain experience, which was already evident at age seven. Nevertheless, a recognized psychosocial onset was independent of gender in

determining the negative impact of pain on the child's daily living and socialization activities.

Key words: pain; gender-roles, psychosocial onset; children

Introduction

Gender differences in the experience of pain are well established in adulthood [1]. Pain is more frequently reported by women, who also describe greater severity and more related disability [2]. This is particularly clear for chronic widespread pain and associated symptoms: in a review of fourteen studies, women had higher prevalence of chronic widespread pain, and in most investigations included it was almost double that observed in men [3].

Gender differences in pain prevalence and prognosis are generally already apparent in childhood and seem to set a life course determination for chronic pain [4, 5]. A study based on a clinic cohort [6] showed that girls were more prone to continuing chronic pain from childhood into adolescence and adulthood. A Dutch population-based study found that 30% of girls reported chronic pain against 20% of boys [7], with girls showing a marked increase in chronic pain report between 12 and 14 years. Concordantly, in a Spanish study with children from ages 8 to 16, the prevalence of chronic pain was also higher in girls than in boys (47% vs 29%) [8]. Petersen et al [9] did not observe gender differences in recurrent headache, stomachache or backache in children from 6 to 13 years old, but found that girls had a higher prevalence of multiple weekly pain. Interestingly, the majority of studies of experimental pain tasks in children did not find differences between genders in pain-related responses [10]. However, studies where the mean age of participants was above 12 years showed some evidence of higher pain intensity, lower tolerance and lower threshold in response to experimental pain among girls[10]. Taken together, this body of evidence supports that the life course experience of chronic pain has gender specificities that become more evident with growth, as both sexual dimorphism and gender roles develop and accentuate.

Previous studies have typically included samples of children of comparatively wide age ranges with corresponding heterogeneity in terms of pubertal and sexual development. This causes comparisons between boys and girls to result from the combined effects of biological and psychosocial differences simultaneously. In order to disentangle the early effect of psychosocial influences such as gender roles (theoretically modifiable) from that of biological sexual dimorphism (essentially non-modifiable), it is crucial to assess children before the onset of puberty, in a period when parental modeling of the pain experience may be a critical influence. This may ultimately contribute to close gender gaps in the knowledge on the etiology of chronic pain throughout life [11].

Therefore, by using data from a large birth cohort, we aimed to assess whether gender differences are already observable in the pain experience of seven-year-old children, specifically regarding parental report, perceived psychosocial triggers and severity of consequences.

Methods

Study design

We conducted a cross-sectional study of children aged seven years taking part of the third wave of evaluation of the Generation XXI (G21) cohort. G21 is a population-based birth cohort that was assembled between November 2005 and August 2006, in five public hospitals providing obstetrical and neonatal care in the metropolitan area of Porto. Mothers were invited to take part in the cohort in the 24-72 hours following birth. Of the invited mothers, 91.4% accepted to participate, which resulted in a baseline sample of 8647 live born infants and 8495 mothers. Detailed methods have previously been described in detail [12]. The study complied with the Ethical Principles for Medical Research Involving Human Subjects expressed in the Declaration of Helsinki and the protocol was approved by the University of Porto Medical School ethics committee and by the National Committee for Data Protection. Written informed consent was obtained from the legal guardian(s) who accompanied each child.

Data collection

Between April 2012 and March 2014, when children were seven years old, the entire cohort was invited to participate in an extensive evaluation including physical examination and face-to-face questionnaires. Of the whole cohort 5843 (61.7%) children attended the scheduled assessment. For the present paper, after excluding nine children with missing information, the sample was composed of 5834 participants, 2840 girls (48.7%) and 2994 boys (51.3%). Respondents were mostly mothers (n=5600) but also fathers (n=152) and other relatives such as grandparents, siblings and aunts (n=82). Since the gender of the respondent was considered an explanatory variable of pain report, sociodemographic background variables and living conditions were compared between groups defined by the respondent (mother, father and other). There were no differences between these groups in parental marital status, existence of siblings, monthly household income, frequency of worry about expenses, caregiver education, parental occupation and child's type of school, hiring a housekeeper, taking holidays away from home and having internet connection. When fathers were the respondents, reporting dampness at home was more common (33.7% vs 26.3%) but having a garden at home was also more frequent (52.2% vs 43.5%).

Pain assessment

Data were collected by trained interviewers in face-to-face assessments. The presence of pain in children in the preceding three months was assessed using a Portuguese version of the Luebeck Pain-Screening Questionnaire (LPQ) applied to the accompanying adult. Since the formal operational stage (notion of time and self-awareness) is not yet fully developed at age seven [13], parents were considered the only valid source of information regarding the presence of pain in children in the preceding three months. The LPQ contained 13 questions. The first was "Did your child complain of pain in the past 3 months?" If the answer was "no", no further questions were asked. If the answer was affirmative, parents were asked to describe the anatomic areas where their child's pain arose and to identify the most important pain according to their own subjective assessment. For that site, duration and frequency data were collected using Likert scales. The intensity of pain was evaluated using a visual analog scale of 1 to 100 mm, anchored with verbal endpoints from "hardly noticeable pain" up to "strongest conceivable pain. Consequences and perceived causes of pain were also evaluated. Moreover, parents were asked if they knew the cause of their child's first episode of pain and whether they had obtained a medical diagnosis for the cause of pain. In addition, a question about history of persistent or chronic pain in the child's family was asked.

Statistical analysis

As for pain features, items of LPQ were categorized as follows, among those who reported any pain in the previous three months:

- Sites: one site, multisite (more than one site);
- Onset: organic onset (illness or injury), psychosocial onset (anxiety, family and school problems, new situations, adverse life events);
- Frequency in the previous three months: low frequency (less than 3 times a month), high frequency (once a week or more);
- Duration: short (less than 3 months), long duration (more than 3 months);
- Intensity: low intensity (from 0 to 50 mm in the VAS), high intensity (over 50 mm).

Consequences of pain in terms of health care, daily living and participation (need of rest, use of medication, visit to the doctor, absence from school, not meeting friends, loss of appetite, sleeping

problems, inability to pursue hobbies and caregiver absence from work) were collected using four-category Likert scales which were aggregated into two categories: never or few times (low impact on daily living) and frequently or always (high impact on daily living). To analyze pain consequences in each gender we selected, among children reporting pain, a key feature that clearly relates to the adult chronic widespread pain syndrome: pain of psychosocial onset vs. organic onset [14, 15].

Absolute and relative frequencies were stratified by gender of the child and of respondent. The statistical significance of differences between groups was assessed using Pearson's chi-squared test. Data were analyzed using the SPSS 22.0 and Stata 11.2.

Results

Presence and features of pain by child gender

Of the overall sample, 44.8% of children were reported by caregivers to have felt pain in the previous three months. Girls were reported to have experienced any pain more frequently than boys (46.7% vs 42.9%, p=0.004). Among children with pain, severity was generally reported as higher in girls: multisite pain was reported for 71.7% of girls and 66.4% of boys (p=0.003), long duration was present in 42.1% of girls and 37.1% of boys (p=0.010), and high frequency was reported for 24.4% of girls and 19.9% of boys (p=0.006). Psychosocial circumstances as triggers of pain onset were also reported more frequently in girls (40.3% against 35.1% of boys, p=0.006). High intensity pain differed little between genders: 17.5% of girls and 16.8% of boys (p=0.660). Regarding the anatomical pain site considered most relevant by respondents (detailed in Supplementary figure 2), there were overall differences between genders (p=0.009), even though the most commonly reported was the abdomen in both genders (23.5% in girls and 22.6% in boys). Lower limb pain was the second most common in boys (22.5% vs 18.4% in girls) whereas in girls headache occupied that position (21.7% vs 20.1% in boys). In addition, 9.5% of girls reported throat pain, against 6.7% of boys, while tooth pain was reported by 10.5% of boys and 8.5% of girls. The most referred perceived causes for pain in boys were physical exertion (26.9%), agitation (21.1%), food/candy (17.8%) and illness (15.2%). In girls these were physical exertion and agitation (21.6%), followed by food/candy (20.9%) and new situations (19.0%). Weather conditions were reported in 16.7% of girls and 12.3% of boys. School work, school problems and nonspecific factors were reported by more than 8.0% of boys and girls. Among children with pain, more girls' than boys' caregivers sought and obtained medical diagnoses (21.5 vs. 18.0%, p=0.026), of which the most common were caries, growth pain, intestinal problems and psychological conditions (such as anxiety and depression).

Maternal vs. paternal pain report

Figure 1A shows the frequency of different pain features in girls and boys according to the caregiver who responded to the questionnaire. In girls, all features were significantly different between respondents: when compared to fathers, mothers more frequently reported any pain (47.4 vs. 31.2%, p=0.002), high intensity (8.3 vs. 4.2%, p=0.007), high frequency (11.6 vs. 9.4%, p=0.006), long duration (20.1 vs. 11.5%, p=0.007), multisite (33.9 vs. 24.0%, p=0.007) and

psychosocial onset (19.3 vs. 9.4%, p=0.005). In boys, the only significant difference between mother and father respondents was regarding pain presence, with mothers reporting any pain more frequently than fathers (43.3 vs. 33.3% p= 0.037). Multisite, high frequency and high intensity pain were also more frequently reported by mothers but the differences were not significant: 28.8% by mothers vs. 22.5% by fathers, p=0.116; 8.7 vs. 4.5%, p=0.079; 7.0 vs. 5.4%, p=0.115, respectively. Long duration and psychosocial onset pain were similar between maternal and paternal reports: 15.8 vs. 15.3%, p=0.068; and 15.0 vs. 14.4%, p=0.073; respectively.

When pain frequency and severity were compared between children's genders within each respondent (Figure 1B), there were no differences in paternal report of pain presence or features according to the child's gender: presence of pain (31.2 in girls vs. 33.3% in boys, p=0.749), multisite (24.0 in girls vs. 22.5% in boys, p=0.679), frequency (9.4 vs. 4.5%, p=245), duration (11.5 vs. 15.3% in boys, p=0.710), intensity (4.2 vs. 5.4%, p=0.900) and psychosocial onset (9.4 vs. 14.4%, p=0.512). However, mothers reported worse symptoms for girls than for boys, regarding frequency (11.6 vs. 8.7%, p<0.001), multisite (33.9 vs. 28.8%, p<0.001), psychosocial onset (19.3 vs 15.0%, p<0.001), duration (20.1 vs. 15.8%, p<0.001) and intensity (8.3 vs. 7.0%, p=0.006).

Psychosocial pain onset and severity outcomes

Among children reporting pain, those whose parents identified a psychosocial trigger were significantly more likely than those with pain of organic onset to present most severity outcomes. This is shown in Table 1 regarding need of rest, use of medication, doctor visit, loss of appetite, sleeping problems and caregiver work absence. However, pain of psychosocial onset had wider-ranging consequences in girls, where it was also associated with absence from school and inability to pursue hobbies, while in boys those associations were not significant. In both girls and boys, associations between psychosocial onset and each consequence were numerically similar regardless of whether the questionnaire was answered by mothers or fathers, even though with lower statistical power in paternal responses.

Family history of chronic pain and child gender

Figure 2 presents the frequency of family history of chronic pain reported by parents of children who had pain. There were no differences in the report of chronic pain between genders (41.5% in girls and 45.2% in boys, p=0.237 for pain of psychosocial onset and 6.6% in girls and 5.5% in boys, p=0.102 for pain of organic onset). Remarkably, chronic pain in the family was much more frequently reported among children whose parents reported pain of psychosocial onset when compared to those reporting pain of organic onset, in both genders (41.5 vs. 6.6%, p<0.001 in girls and 45.2 vs. 5.5%, p<0.001 in boys). The most frequently identified family members with chronic pain were mothers (45.0%), followed by grandmothers (25.8%) and fathers (16.5%).

Discussion

In this study, gender shaping of the pain experience was already evident at age seven: an interaction between parental and offspring genders seems to be a key influence on the reporting of pain, since mothers of girls reported higher frequency and worse severity than mothers of boys or fathers of children of both genders. However, when examining pain of psychosocial onset in particular, there were relevant similarities between girls and boys: family history of chronic pain was a marker of the probability of reporting psychosocial pain triggers in both genders. Also, regardless of the respondent, pain of psychosocial onset was associated with worse reported consequences in both genders but more extensively among girls.

We found clear differences between girls and boys with regard to the frequency of any pain as well as to the severity of the symptom. This is in agreement with previous literature: the study of Haraldstad, Sorum [16] girls reported more pain than boys (65.0% vs 55.0%) although differences in pain features were not present. Perquin (2000) [7] and Roth-Isigkeit, Thyen [17] found similar results with our study in terms of higher report of pain, multisite, high intensity and high frequency, which is consistent with studies in adulthood [18].

Our study extends existing evidence by adding a key gender interaction on the estimation of the frequency and severity of pediatric pain since an early age. Generation XXI mothers reported their offspring had felt pain more frequently than fathers, regardless of the child's gender. The accuracy of symptom report from parents depends on several issues, of which the role and presence as a caregiver are particularly important and suggest higher sensitivity of maternal report with regard to the recognition of pain symptoms in the child. This is in agreement with Barak et al (2008) [19] and Morrow et al (2010) [20] which found that the primary caregiver, usually mothers, have an accurate pain perception of their child. Also, the emotional connection between the mothers and children and their proximity affects perceptions of emotional indicators and of pain experienced by the child [21], which indicate that mothers may be the best informants of pain levels experienced by their children.

Nevertheless, our observation that mothers tended to report pain more frequently among their female rather than male offspring is striking, especially when seen at the light of an absence of gender differences when fathers were asked to report on their child's pain symptoms. This parent-child gender interaction could be interpreted as mothers being more able to accurately distinguish

existing gender differences in the pain experience of young children, in which case they would be a more accurate source to capture the child's pain experience. This would imply that gender disparities in the pain experience are at least partly established by age seven. Considering this, it is possible to explain those disparities by three potential mechanisms [22]: experiential (e.g. learning about pain and identification with gender roles), biological (e.g. hormones, contact with pathological agents) and psychosocial mechanisms (e.g. attitudes towards pain). Regarding the experiential mechanism (gender-role), pain expression is more acceptable in girls than in boys and parental socialization processes may be more accepting or even encouraging of pain expression by girls [6, 13, 23]. Biological explanations may be related to a lower pain threshold in females due to the differences in sex hormones after puberty [6], to differences in perception and reaction to emotional stimuli [24] and to lower pain tolerance and greater unpleasantness [22]. Generally, women tend to react more to negative stimuli and this is true in girls from 7 to 10 years [25], which suggests that stimuli may activate different neurocircuitry in men and women, resulting in differences in pain modulation due to divergent emotional experiences [24]. Psychosocial mechanisms can be related to the fact that women may be more attentive to health disturbances than men [13]. However, we cannot exclude the possibility that the child's gender has a causal influence on maternal report independently of the true frequency or severity of the symptom. This alternative is supported by the similarity found between girls and boys when pain features were reported by fathers. Due to the young age of the Generation XXI children, we were not able to test parental against child's report of symptoms. But, regardless of whether the most valid estimates are obtained by questioning mothers or fathers, gender interaction between children and caregivers seems very likely to interfere with the child's modeling of pain, possibly into adulthood. This finding is particularly important due to the time frame considered here, since children were evaluated largely before the onset of pubertal development. This suggests that gender heterogeneity is more likely to begin as a result of psychosocial influences, possibly within the immediate family, than due to different neurohormonal environments that would modulate the physiological pain response - which seem to be clearer after 12 years of age [10].

An important limitation of our study in this regard was the fact that only one of the caregivers was questioned about each child's symptoms, and therefore our comparisons assume the similarity (exchangeability) between children whose questionnaires were answered by mothers and by fathers. This is supported by our observation that there were no major sociodemographic or economic differences by respondent, even though we cannot exclude some degree of unmeasured bias.

Another relevant finding concerning transgenerational aspects was the clear association between family history of chronic pain and the interpretation of the child's pain as a result of psychosocial distress. Pain of psychosocial onset in childhood is a known risk marker for the development of the chronic widespread pain syndrome in adulthood [26, 27], and the association of this indicator with a family history of chronic pain is striking. If, on the one hand, this association might translate genetic predisposition to an altered pain response, on the other hand it may reflect an influence of parental modeling of their own pain experience on the child's pain behavior (or the recognition of such response by parents) [28, 29]. Importantly, this observation was common to girls and boys, which supports partly independent but reinforcing roles for gender and family influences on the pain experience.

Also consistently between girls and boys, pain for which parents recognized a psychosocial onset was clearly associated with worse outcomes, in terms of healthcare use, well-being and social participation. This shows that the influence of psychosocial context starts developing early in life, and supports the important cultural and social influence in pain perception [29]. Although associations were more extensive in girls, these findings generally validate poorer responses to psychosocial distress as an early marker of somatic symptoms with disabling consequences that become manifest even before the first decade of life is completed.

Our investigation showed an interaction between parental and offspring genders on the report of the pain experience, which was already evident at age seven. Nevertheless, a recognized psychosocial onset was independent of gender in determining the negative impact of pain on the child's daily living and socialization activities.

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Tables and figures

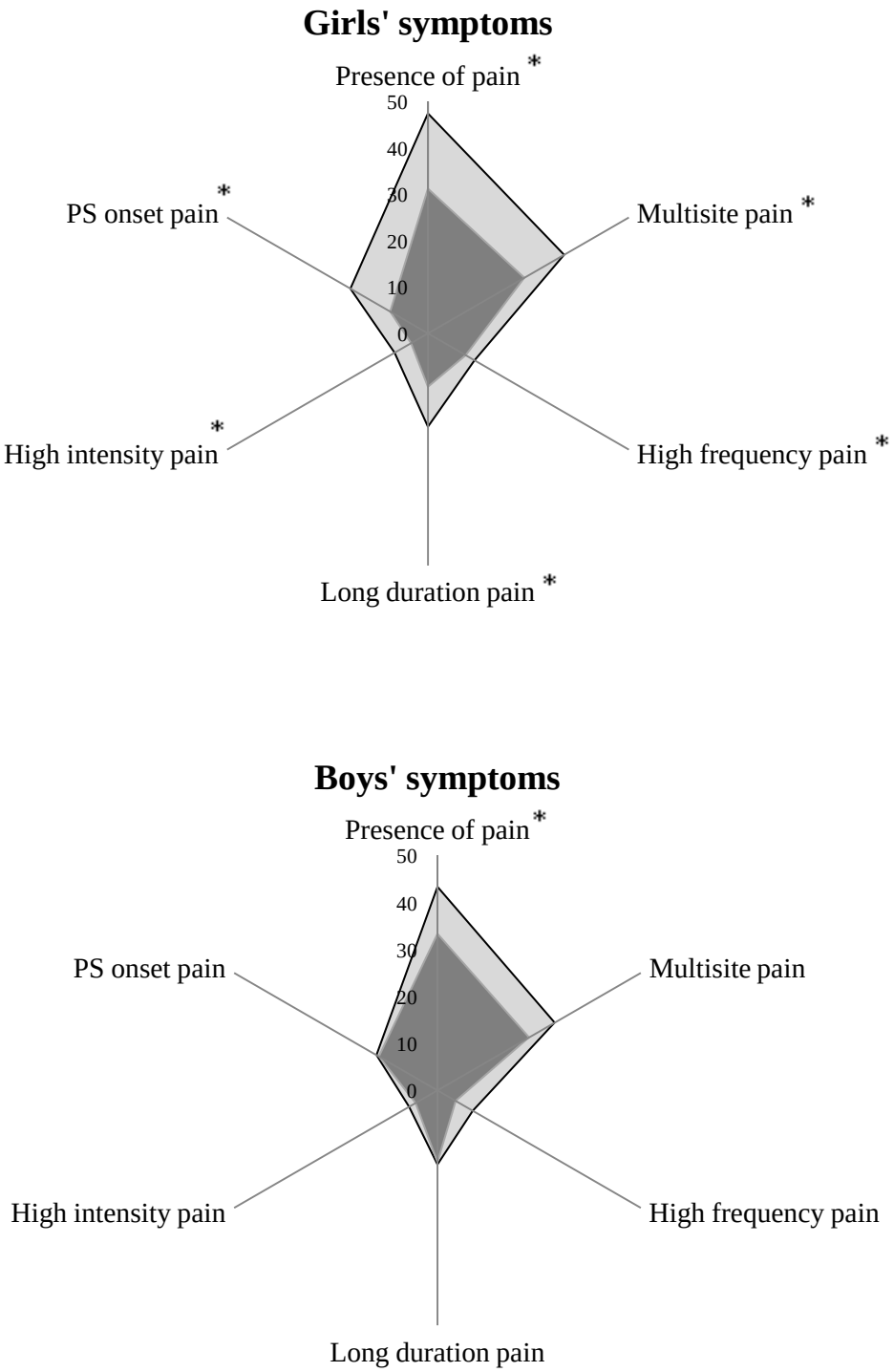


Figure 1A – Frequencies (%) of pain and its features in the previous three months (using the whole sample as denominator) according to respondent's gender, in girls (n=2782, mother respondent: 2686, father respondent: 96) and boys (n= 2938, mother respondent: 2827, father respondent: 111). Black line: mother respondents, Grey line: father respondents. PS: psychosocial (features with * showed statistically significant differences between respondents, $p<0.05$).

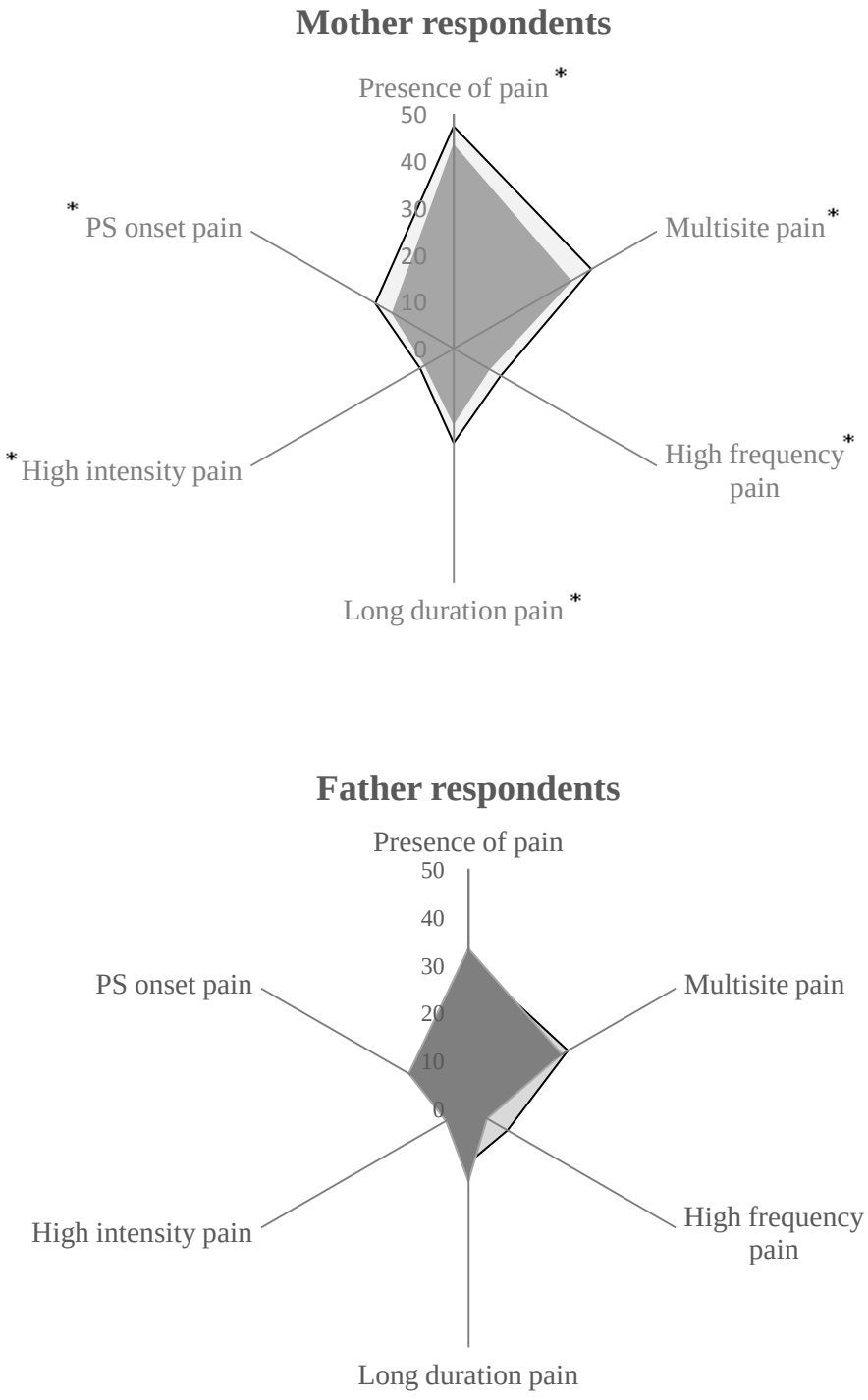


Figure 1B – Frequencies (%) of pain and its features in the previous three months (using the whole sample as denominator) according to child's gender, when mothers (n=5513, girls: 2686, boys: 2827) or fathers (n= 207, girls: 96, boys: 111) were the respondents. Black line: girls, Grey line: boys. PS: psychosocial (features with * showed statistically significant differences between respondents, $p<0.05$).

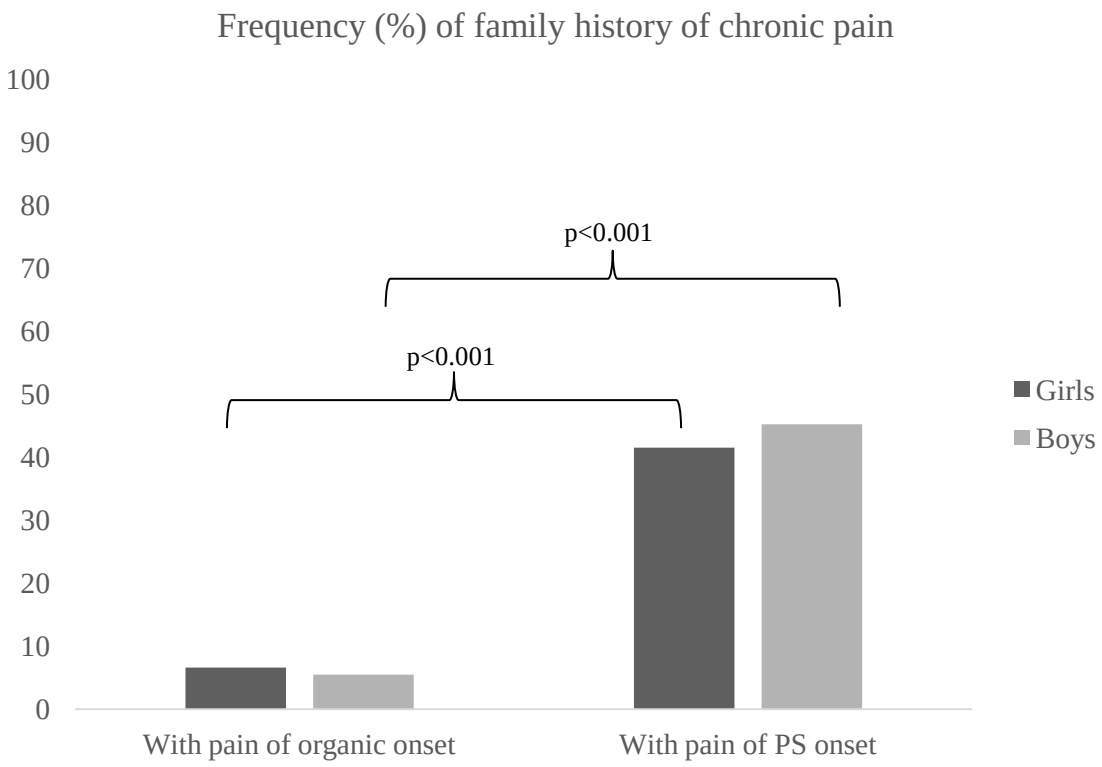
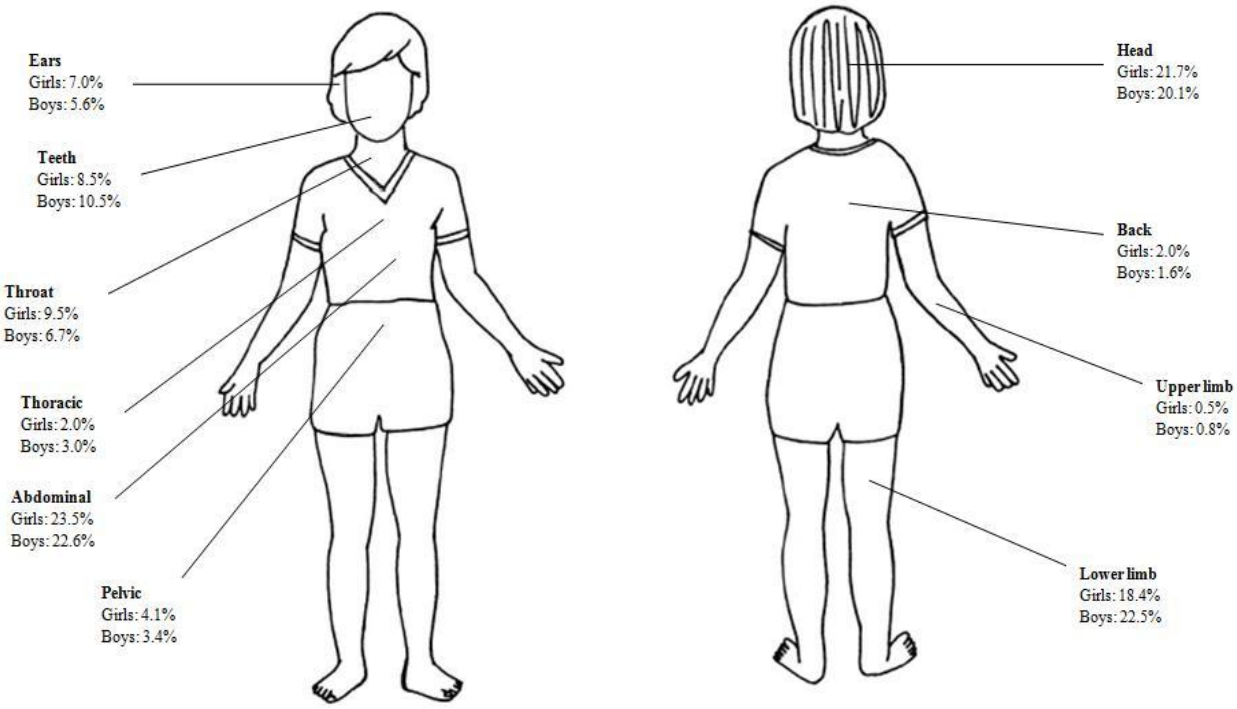


Figure 2 – Frequency (%) of family history of chronic pain among children reporting pain of organic and psychosocial (PS) onset, by gender of the child.

Table 1 – Frequencies of different pain consequences according to the trigger - psychosocial vs. organic onset - in girls and boys.

	Girls			Boys		
Pain consequences	**Psychosocial onset (n=533)**	**Organic onset (n= 788)**	**p**	**Psychosocial onset (n= 449)**	**Organic onset (n= 829)**	**p**
Needed of rest						
Never or few times	439 (82.4)	732 (92.9)	<0.001	362 (80.6)	779 (94.0)	<0.001
Frequently or always	94 (17.6)	56 (7.1)		87 (19.4)	50 (6.0)	
Use of medication						
Never or few times	451 (84.6)	731 (92.9)	<0.001	376 (83.7)	769 (92.8)	<0.001
Frequently or always	82 (15.4)	57 (7.2)		73 (16.3)	60 (7.2)	
Visit to the doctor						
Never or few times	484 (90.8)	756 (95.9)	<0.001	404 (90.0)	789 (95.2)	<0.001
Frequently or always	49 (9.2)	32 (4.1)		45 (10.0)	40 (4.8)	
Absence from school						
Never or few times	517 (97.0)	780 (99.0)	0.008	435 (96.9)	812 (97.9)	0.236
Frequently or always	16 (3.0)	8 (1.0)		14 (3.1)	17 (2.1)	
Not meeting friends						
Never or few times	523 (98.1)	778 (98.7)	0.375	437 (97.3)	816 (98.4)	0.174
Frequently or always	10 (1.9)	10 (1.3)		12 (2.7)	13 (1.6)	
Loss of appetite						
Never or few times	477 (89.5)	760 (96.4)	<0.001	394 (87.8)	790 (95.3)	<0.001
Frequently or always	56 (10.5)	28 (3.6)		55 (12.2)	39 (4.7)	
Sleeping problems						
Never or few times	486 (91.2)	759 (96.3)	<0.001	405 (90.2)	801 (96.6)	<0.001
Frequently or always	47 (8.8)	29 (3.7)		44 (9.8)	28 (3.4)	
Unable to pursue hobbies						
Never or few times	498 (93.4)	770 (97.7)	<0.001	430 (95.8)	804 (97.0)	0.255
Frequently or always	35 (6.6)	18 (2.3)		19 (4.2)	25 (3.0)	
Caregiver missed work						
Never or few times	504 (94.6)	766 (97.2)	0.014	427 (95.1)	808 (97.5)	0.025
Frequently or always	29 (5.4)	22 (2.8)		22 (4.9)	21 (2.5)	



Supplementary figure 1 – Frequencies (%) of the most impairing pain location, in boys and girls.

ChapterII

Socioeconomic context, living conditions and the pediatric pain experience: parental report of chronic widespread pain features in 7-year-old children

Abstract

Background: Chronic widespread pain has great individual and population impact**.** The mechanisms that originate pain behavior and suffering are shaped throughout the life course. This theoretical model is consistent with empirical observations that prior pain experience is the main risk marker for a new episode of pain. Throughout the life course, the determinants of pain experience are thought to act at different, nested levels, from individual to contextual influences, ranging from psychosocial context to sociodemographic characteristics.

Objective: To assess whether psychosocial context predicts features of pediatric pain that overlap the chronic widespread pain syndrome from as early as age seven.

Methods: We used data from 5834 seven year old children from Generation XXI cohort. Pain was assessed using the Portuguese version of Luebeck Pain Screening Questionaire. Individual characteristics were assessed through questionnaires applied in individual interviews. The statistical significance of differences in proportions between groups was assessed using Pearson's chi-squared test. To estimate the associations of contextual and individual variables with three study outcomes, logistic regression was conducted, comparing: 1) children with pain complaints in the preceding three months versus the remaining children; 2) children with psychosocial events for the onset of pain versus all the remaining children, and 3) children with multisite pain versus all the remaining children.

Results: Psychosocial circumstances at the onset of pain were identified by 16.9% of parents. All characteristics showed significant differences by gender: with girls' caregivers reporting worse pattern of pain. Sociodemographic background variables were not significantly associated with pain in either gender. Recent pain report was not associated with social support indicators, in either gender. However, indicators of living conditions showed a social gradient in both genders with regard to different pain outcomes: girls and boys who did not have a garden at home were significantly more likely to be reported to complain of pain of psychosocial onset (girls: OR= 1.380, 95% CI: 1.137, 1.674; boys: OR= 1.220, 95% CI: 0.994, 1.498). Girls whose family did not hire a housekeeper had higher odds of pain of psychosocial onset (OR= 1.364, 95% CI: 1.039, 1.791). Both boys and girls whose parents reported dampness or mold at home

were more likely to report all pain outcomes: any pain (girls: OR= 1.246, 95% CI: 1.054, 1.474; boys: OR= 1.332, 95% CI: 1.132, 1.569), multisite pain (girls: OR= 1.306, 95% CI: 1.097, 1.556; boys: OR= 1.362, 95% CI: 1.103, 1.681) and pain of psychosocial onset (girls: OR= 1.267, 95% CI: 1.030, 1.560; boys: OR= 1.308, 95% CI: 1.052, 1.627).

Conclusion: In conclusion, at seven years of age, poor living conditions were associated with parental report of multisite pain and pain of psychosocial onset. These seemed to be independent of classic indicators of deprivation and social support, suggesting that this might be a key stage in life to prevent an adverse socioeconomic patterning of the pain experience.

Key words: Chronic widespread pain, children, living conditions, psychosocial onset pain, multisite pain

Introduction

Chronic widespread pain has great individual and population impact, since it is highly frequent and affects virtually all dimensions of an individual's functioning, from personal to societal levels [1]. Research over the past two decades has been instrumental in bringing together the neurochemical and psychosocial models of chronic pain, namely through clarifying central sensitization [2]. Central plasticity provides mechanistic support for the chronic widespread pain manifestation as a key feature of the fibromyalgia syndrome, which in turn gains nosological meaning beyond a diagnosis of exclusion.

From the population point of view, epidemiologic research has added crucial elements to the understanding of chronic widespread pain. One of the most relevant is that the mechanisms that originate pain behavior and suffering are shaped throughout the life course. This theoretical model is consistent with empirical observations that prior pain experience is the main risk marker for a new episode of pain [3, 4, 5]. In a Finnish study, more than half of participants reporting musculoskeletal pain in childhood reported similar symptoms four years later in adolescence [6]. Another work found that near 30% of children reporting pain will grow up to be adolescents with chronic pain [7]. Brattberg [8] observed that 59% of women and 39% of men who reported pain in childhood also reported it in early adulthood. Moreover, Jones *et al* [9] found that children aged 7 who were reported by their mothers to complain of multiple childhood symptoms were 1.5 times more likely to have CWP at age 45. This also highlights that, during the first decade of life, the observable dimension of pediatric pain results from a shared experience that features an interaction between the child's patent distress and the parental attitude towards pain.

Throughout the life course, the determinants of pain experience are thought to act at different, nested levels, from individual to contextual influences. Psychosocial context, in particular, may modulate the likelihood that injury or illness will promote plastic changes at the central nervous system level that make the individual more prone to develop chronic widespread pain [10]. This is compatible with observations that behavioral and emotional factors are implicated in the process of central sensitization [11, 12]. For instance, parental modeling of illness behavior can lead to poor pain perception and coping in adulthood which is associated with increased vulnerability to chronic pain development [13, 14]. Prospective studies have also shown that adverse early life events, such as hospitalization after an accident or contextual changes such as separation from mothers, are also associated with CWP [15, 16]. Other family-level determinants of chronic pain have been identified, such as abuse or neglect [17]. At an upstream level, socioeconomic context, is also a well-known correlate of chronic pain, possibly in part as a marker of psychological

distress. Deprivation indicators such as education, employment status and neighborhood socioeconomic status have all been found to be associated with the likelihood of developing chronic widespread pain [18].

Concerning the role of context over the life course key issues remain to be clarified, including how early in life the psychosocial shaping of the pain experience begins, whether socioeconomic and psychological dimensions have similar importance. Therefore, using gender-specific data reported by parents from a large population-based birth cohort, we aimed at assessing whether psychosocial context predicts features of pediatric pain that overlap the chronic widespread pain syndrome from as early as age seven.

Methods

Study design

We conducted a cross-sectional study of children aged 7 years taking part of the third wave of evaluation of the Generation XXI (G21) prospective cohort study. G21 is a population-based birth cohort that was assembled between November 2005 and August 2006, in five public hospitals providing obstetrical and neonatal care in the metropolitan area of Porto, Portugal. Mothers were invited to take part in the cohort in the 24-72 hours following delivery. Of the invited mothers, 91.4% accepted to participate, which resulted in a baseline sample of 8647 live born infants and 8495 mothers. Detailed recruitment methods have previously been described in detail [19]. Between April 2012 and March 2014, when children were 7 years old, the entire cohort was invited to participate in another extensive evaluation including physical examination and face-to-face questionnaires. Of the whole cohort 5843 (61.7%) children accepted to participate and attended the scheduled assessment. Data were collected by trained interviewers in face-to-face assessments. The study complied with the Ethical Principles for Medical Research Involving Human Subjects expressed in the Declaration of Helsinki. The protocol was approved by the University of Porto Medical School ethics committee and by the National Committee for Data Protection. Written informed consent was obtained from the legal guardian(s) who accompanied each child and assent was obtained from the child.

Pain assessment

History of pain complaints by the child in the preceding three months was assessed using a Portuguese version of the Luebeck Pain-Screening Questionnaire (LPQ) applied to the accompanying adult (the mother in 95% of participants). Since the formal operational stage (notion of time and self-awareness) is not yet fully developed at age 7 [20], parents were considered the most valid source of information regarding the presence of pain in children in the preceding three months. The LPQ contains between one and 13 questions (figure 1). The first question was “Did your child complain of pain in the past 3 months?” If the answer was “no”, no further questions were asked. If the answer was affirmative, parents were asked to describe the anatomic areas where their child felt pain and to identify the most important pain according to their own subjective assessment. Regarding that site, Likert scales were used to collect information on duration and frequency. The intensity of pain was evaluated using a visual analog

scale of 1 to 100 mm, anchored with verbal endpoints ("hardly noticeable pain" to "strongest conceivable pain"). Consequences and perceived causes of pain were also collected. Moreover, parents were asked if they knew the cause of their child's first episode of pain and whether they had obtained a medical diagnosis for the cause of pain. In addition, a question about history of persistent or chronic pain in the child's family was asked. Items of LPQ related to pain characteristics were categorized as follows:

- Sites: one site or multisite;
- Onset: organic (due to illness or injury) or psychosocial onset (due to anxiety, family and school problems, new situations, adverse life events or no apparent reason);
- Frequency in the previous three months: low (less than 3 times a month) or high frequency (once a week or more);
- Duration: short (less than 3 months) or long duration (more than 3 months);
- Intensity: low (from 0 to 50 mm in the VAS) or high intensity (over 50 mm).

Exposure assessment

Variables presented in the literature as possible contributors to the onset of pain in children and adult populations were considered. Parental background socioeconomic position indicators were education (schooling of the main caregiver), employment status, monthly household income, frequency of worry about expenses, and type of school that the child attended at age seven (public vs. private). Living conditions included having a garden at home, hiring a housekeeper, having dampness or mold at home, having internet access from home, and taking holidays away from home. Social support data included belonging to an organized sports team, having music lessons and attending religious activities. Family structure was assessed by inquiring parental marital status and presence of siblings. Indicators of psychosocial distress collected were history of suspicion or diagnosis of behavioral or socialization problems.

Statistical analysis

All analyses were stratified by gender. The statistical significance of differences in proportions between groups was assessed using Pearson's chi-squared test. On the basis of the current model of chronic widespread pain, we considered three pain outcomes: any pain in the previous three months, multisite pain and pain of psychosocial onset. To estimate the associations of contextual

and individual variables with these three features logistic regression was conducted, comparing: 1) children with pain complaints in the preceding three months versus the remaining children; 2) children with psychosocial events for the onset of pain versus all the remaining children (no pain or pain with organic causes of onset), and 3) children with multisite pain versus all the remaining children (no pain or one pain site). Data were analyzed using Stata 11.1 and SPSS 22.0.

Results

The sample was composed of 2833 girls (48.7%) and 2981 boys. The presence of any pain in the previous 3 months as reported by parents was 44.8% in the whole sample. Multisite pain was present in 30.9% of children and 17.7% of parents reported chronicity. Psychosocial circumstances at the onset of pain were identified by 16.9% of parents. As presented in Figure 1, all characteristics showed significant differences by gender: more girls than boys had multisite (33.5% vs. 28.4%, p<0.001), high frequency (11.4% vs. 8.5%, p<0.001), long duration (19.6% vs. 15.9%, p<0.001) and high intensity pain (8.2% vs. 7.0%, p=0.010). Also, more girls' caregivers identified pain of psychosocial onset (18.8% vs. 15.1%, p<0.001).

Tables 1 and 2 present the associations between indicators of psychosocial context and pain outcomes in girls and boys, respectively. In general, sociodemographic background variables were not significantly associated with pain in either gender, including parental marital status, parental educational level, household income and child's school type. Girls who with siblings had lower odds of reporting pain of psychosocial onset (OR= 0.782; 95% CI= 0.646; 0.948), whereas boys whose parents were employed part-time showed lower odds of multisite pain (OR= 0.711; 95% CI= 0.510; 0.991) but these associations were not replicated for the remaining pain outcomes. Similarly, recent pain report was not associated with social support indicators such as belonging to a sports group or team, engaging in group music activities or joining religious activities in either gender.

However, when indicators of living conditions were analyzed, as shown in Figure 2, there seemed to be a social gradient in both genders with regard to different pain outcomes: girls and boys who did not have a garden at home were significantly more likely to be reported to complain of pain of psychosocial onset (girls: OR= 1.380, 95% CI: 1.137, 1.674; boys: OR= 1.220, 95% CI: 0.994, 1.498). Girls whose family did not hire a housekeeper had higher odds of pain of psychosocial onset (OR= 1.364, 95% CI: 1.039, 1.791) whereas higher odds of any pain and multisite pain were found in boys (OR= 1.658, 95% CI: 1.370, 2.006 and OR= 1.362, 95% CI: 1.103, 1.681, respectively). Remarkably, both boys and girls whose parents reported dampness or mold at home were more likely to report all pain outcomes: any pain (girls: OR= 1.246, 95% CI: 1.054, 1.474; boys: OR= 1.332, 95% CI: 1.132, 1.569), multisite pain (girls: OR= 1.306, 95% CI: 1.097, 1.556; boys: OR= 1.362, 95% CI: 1.103, 1.681) and pain of psychosocial onset (girls: OR= 1.267, 95% CI: 1.030, 1.560; boys: OR= 1.308, 95% CI: 1.052, 1.627). Additionally, boys whose family did not take holidays away from home were more likely to parent report of any pain (OR= 1.429,

95% CI: 1.208, 1.691). Internet availability was not clearly associated with pain report, except in girls, where the absence of connection at home was inversely associated with psychosocial pain.

As for indicators of psychosocial distress, no clear associations were found with pain outcomes for socialization problems or weight problems. There was a borderline significant direct association between parental report of behavior problems and pain of psychosocial onset in girls (OR= 1.306, 95% CI: 0.999, 1.707).

Sensitivity analysis was performed to assess if there were differences in the findings when only mothers answered to the questionnaires. We did not find any differences in the relationships between the analyzed variables.

Discussion

In a cohort of children born in 2005/6, chronic widespread pain features – multisite symptoms and psychosocial onset - were already present in both genders at age seven. Multisite pain and pain with psychosocial onset were clearly more associated to material living conditions than to classic socioeconomic indicators and individual-level characteristics.

Previous studies on chronic widespread pain in children have found low prevalence estimates, with prevalence ranging from 2 to 6 % of school-aged children [21, 22]. Nevertheless, it is widely accepted that adverse experiences in childhood set pediatric origins for chronic widespread pain in adulthood. Some prospective studies have shown that adverse early life events, such as hospitalization after accident or separation from mothers as well as abuse or neglect, are associated with chronic widespread pain [15-17]. Also, parental modeling of illness behavior can lead to poor pain perception and coping in adulthood which is associated with increased vulnerability to chronic pain development [13, 14]. However, most research has included comparatively small samples of children of wider and more advanced age ranges. Additionally, many previous studies were not specifically directed to the study of pain features that overlap the adult chronic widespread pain syndrome. Our investigation provides important population-based evidence to support that key features such as multisite and psychosocial onset pain are present from age seven. In addition, we were able to use a wide range of socioeconomic and psychological indicators to explore psychosocial determinants of the experience of those features from a very early age.

In adults, the relation between socioeconomic factors and pain is evident: lower socioeconomic status is associated with increased risk of pain, in all continents and both in community samples [23] and clinical settings [24]. This deprivation-related risk may be mediated by psychological distress, through less effective coping strategies (catastrophizing, praying and hoping) used by individuals with lower educational level [18]. Lower socioeconomic position may also influence the risk of pain onset through the quantity and quality of interpersonal relationships, i.e. social support [18]. This emphasizes the importance of addressing the timing during the life course when effects of socioeconomic context become apparent.

In the Generation XXI children, classic socioeconomic markers, such as caregiver's education and monthly household income, did not show significant associations with multisite or psychosocial onset pain which is congruent with the studies of Jones et al (2007) [9] and

Mikkelsson (2008) [25]. However, we found striking associations between material living conditions and pain frequency and features in children: psychosocial onset pain was associated with having a garden at home in both genders and, in girls, also with hiring a housekeeper. In boys, any and multisite pain were associated with hiring a housekeeper whereas taking holidays away from home was associated with higher odds of any pain. Importantly, parents who reported dampness or mold at home were more likely to report that their child had complained of any, multisite and psychosocial onset pain, and this relation was present for both girls and boys. These results are in line with those found by Ostberg et al in Sweden, where economic stress but not social class were associated with psychosomatic complaints in school-aged children [26]. The interpretation of such findings is not straightforward. On the one hand, our measures of material deprivation may reflect a further stratification of families within categories of classic socioeconomic indicators, meaning that they would work as a finer proxy of overall social environment. In this case, socioeconomic deprivation would be associated with increased risk of pain report from the first decade of life. On the other hand, a more likely explanation may be that material living conditions influence psychological well-being independently of background socioeconomic position, with the latter being less relevant as a modulator of the pain experience at this life stage. Housing is considered a strong determinant of population health [27] and housing conditions are related to health and well-being regardless of individual features [28]. Poor housing conditions affect people's health status, physically and mentally, family relationships and the conduct of basic social activities, such as inviting people at home [29, 30]. There is evidence that the existence of dampness and mould is associated with mental illness [30]. A study in Glasgow [31] found that the presence of dampness at home was significantly and independently associated with scoring more than 5 on the General Health Questionaire for assessing mental health. Also, anxiety and depression showed an association with the number of housing problems [30]. Moreover, family and neighborhood living conditions, such as exposure to adversity (particularly the sustained, unmediated adversity producing "toxic stress") becomes biologically embedded, influencing gene expression and brain development [32]. Confounding factors regarding house conditions may be related to the effects of housing in the individuals, leaving them with lower resistance to physical and mental illness because of living in a poor, stressful and uncongenial place; due to unhealthy habits (possibly negative coping strategies); and to reduced self-organization [33].

Another relevant finding was the lack of associations between social support indicators (musical, religious or sports activities) and all pain outcomes, in both genders. Taken together with the observations above, this might be explained by a predominance of household influence on pain

symptoms at this age over a wider social context beyond the immediate family [34]. This would be supported by our observation of lower odds of psychosocial onset pain among girls with siblings, even though no associations were found in boys.

An important limitation of our study is that we did not collect specific measures of psychological distress in children, which would be essential to clarify the mechanisms underlying the association between material living conditions and pain report. Our closest proxy was parental report of behavior and socialization problems. In that regard, psychosocial onset pain in girls was associated with behavioral problems, but no other associations were found.

The major strength of this study is the large population-based sample of children with the same age, at a very early stage of life. Also, to our knowledge this is the first study to analyze, in a community-based sample of children, key features of the chronic widespread pain syndrome (multisite and psychosocial onset pain) in relation to socioeconomic indicators and material living conditions. Nevertheless, it should be noted that many of the exposures reported by parents may not have been collected with optimal validity since they are subject to some degree of social desirability bias. In the case of a true socioeconomic patterning of pediatric pain, this would probably contribute to attenuate the associations measured.

In conclusion, at seven years of age, poor living conditions were associated with parental report of multisite pain and pain of psychosocial onset. These seemed to be independent of classic indicators of deprivation and social support, suggesting that this might be a key stage in life to prevent an adverse socioeconomic patterning of the pain experience.

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Tables and figures

Figure 1. Distribution (%) of 7-year-old boys and girls according to the characteristics of the most relevant pain in the preceding three months as reported by parents.

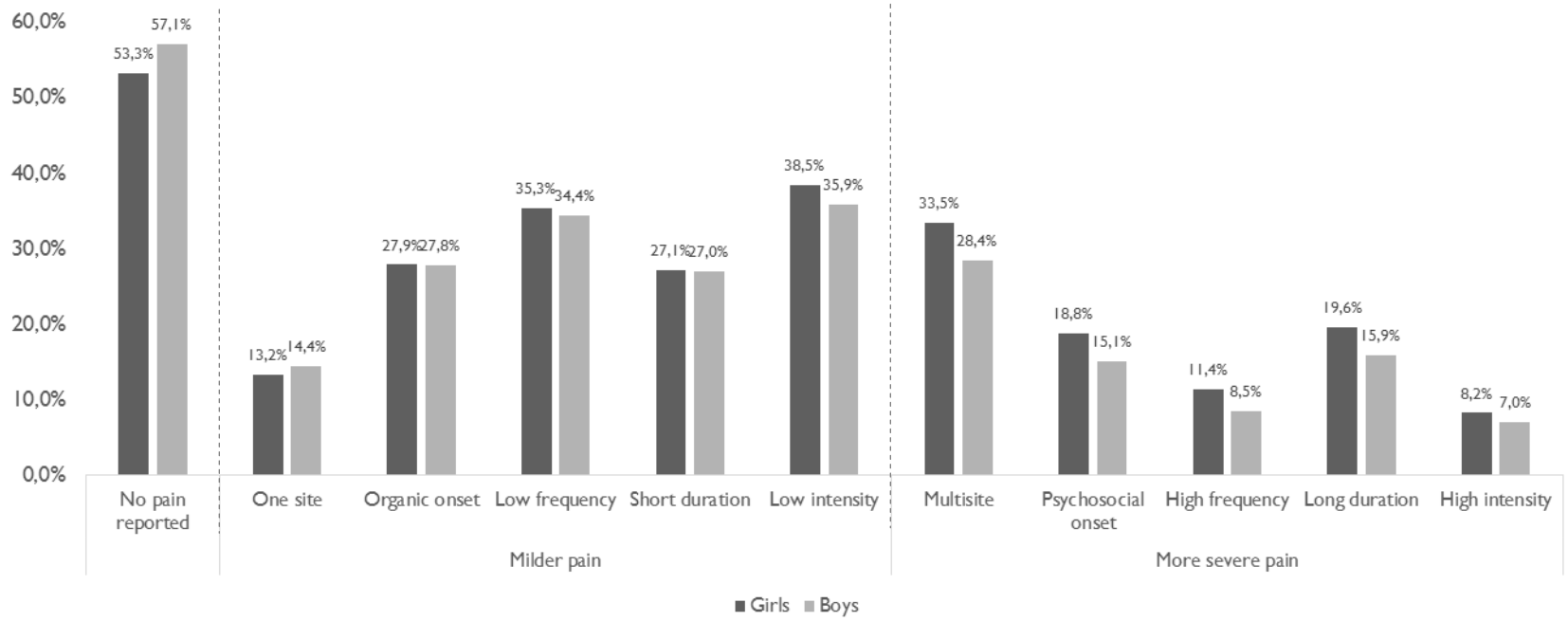


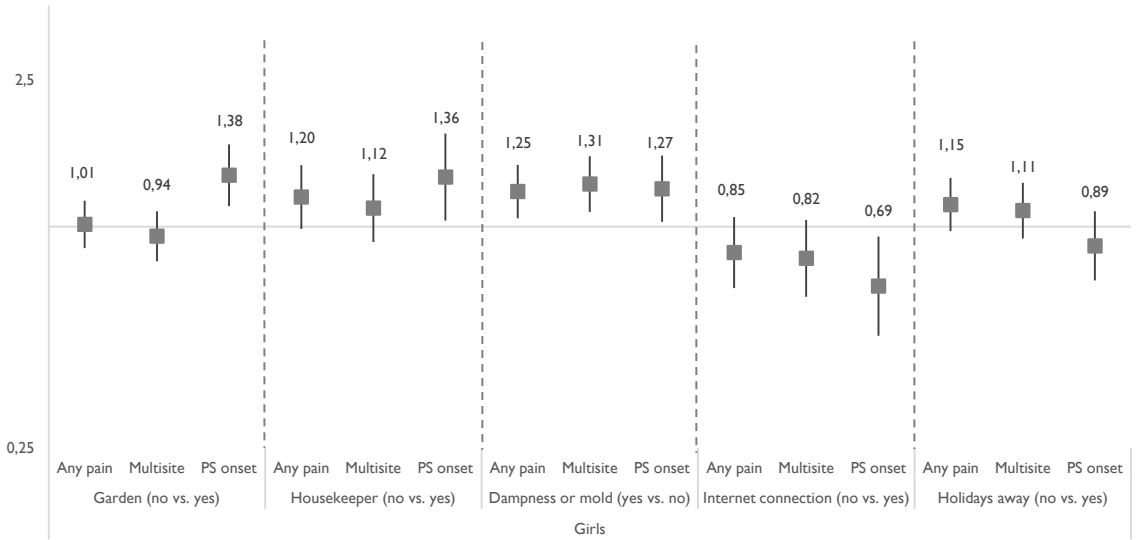
Table 1. Distribution and associations (odds ratios and 95% confidence intervals) between indicators of psychosocial context and pain outcomes in girls: any pain, multisite pain and pain of psychosocial onset.

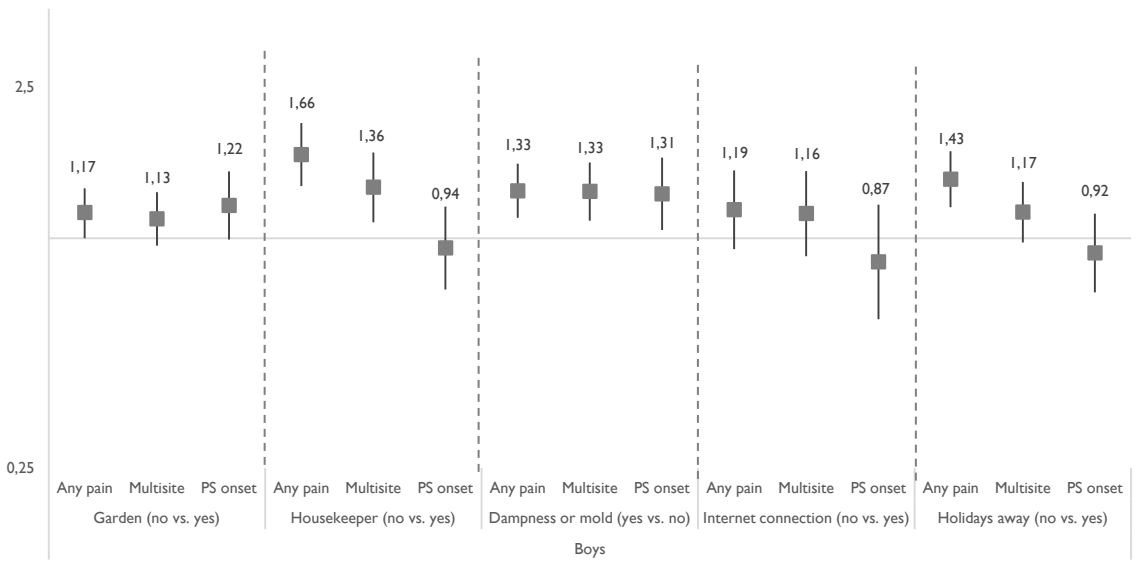
	Sample distribution	Any pain	Multisite	Psychosocial onset
	n (%)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Sociodemographic background				
Parental marital status				
Together	2442 (86.3)	1	1	1
Separated	387 (13.7)	1.103 (0.890; 1.367)	1.163 (0.930; 1.455)	1.158 (0.888; 1.512)
Siblings				
No	1081 (38.2)	1	1	1
Yes	1752 (61.8)	0.987 (0.848; 1.149)	0.978 (0.833; 1.149)	0.782 (0.646; 0.948)
Caregiver educational level				
Basic	1249 (44.1)	1	1	1
Secondary	855 (30.2)	0.861 (0.723; 1.025)	0.858 (0.712; 1.034)	0.865 (0.690; 1.085)
Higher	729 (25.7)	0.897 (0.747; 1.077)	1.065 (0.879; 1.289)	0.949 (0.752; 1.198)
Monthly household income (Euro)				
≤ 1000	912 (33.0)	1	1	1
1001 – 2000	1295 (46.8)	0.924 (0.780; 1.094)	0.957 (0.800; 1.145)	0.841 (0.677; 1.045)
2001 – 3000	409 (14.8)	0.787 (0.622; 0.996)	0.900 (0.702; 1.155)	0.881 (0.653; 1.188)
>3000 €	151 (5.5)	0.848 (0.600; 1.199)	0.928 (0.643; 1.340)	1.043 (0.683; 1.594)
Parental occupation				
Full-time	1870 (66.1)	1	1	1
Part-time	230 (8.1)	1.042 (0.792; 1.371)	1.117 (0.839; 1.486)	1.152 (0.819; 1.618)
Unpaid	729 (25.8)	0.978 (0.823; 1.160)	0.947 (0.789; 1.136)	0.972 (0.779; 1.213)
Concern about household expenses				
Never or rarely	158 (5.6)	1	1	1
Sometimes or a lot of times	615 (21.9)	1.252 (0.879; 1.783)	1.226 (0.837; 1.797)	1.142 (0.724; 1.802)
Almost always or always	2040 (72.5)	1.237 (0.891; 1.716)	1.247 (0.874; 1.779)	1.027 (0.671; 1.573)
Child's school type				
Private	243 (8.6)	1	1	1
Public	2576 (91.4)	1.161 (0.890; 1.513)	1.088 (0.820; 1.443)	0.982 (0.703; 1.372)
Social support				
Sports in a group or club				
No	2195 (77.6)	1	1	1
Yes	632 (22.4)	0.919 (0.769; 1.098)	1.148 (0.954; 1.382)	0.887 (0.704; 1.119)
Music activities				
No	2538 (89.6)	1	1	1
Yes	295 (10.4)	0.835 (0.655; 1.066)	0.800 (0.614; 1.042)	0.887 (0.645; 1.221)
Religious activities				
No	895 (31.6)	1	1	1
Yes	1937 (68.4)	0.893 (0.762; 1.047)	0.980 (0.829; 1.159)	0.991 (0.809; 1.215)
Psychosocial distress				
Behavior problems				
No	2455 (87.3)	1	1	1
Yes	357 (12.7)	1.002 (0.802; 1.252)	1.037 (0.820; 1.311)	1.306 (0.999; 1.707)
Socialization problems				
No	2645 (94.0)	1	1	1
Yes	170 (6.0)	1.240 (0.909; 1.692)	1.215 (0.882; 1.674)	1.168 (0.797; 1.712)

Table 2. Distribution and associations (odds ratios and 95% confidence intervals) between indicators of psychosocial context and pain outcomes in boys: any pain, multisite pain and pain of psychosocial onset.

	Sample distribution	Any pain	Multisite	Psychosocial onset
	n (%)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Sociodemographic background				
Parental marital status				
Together	2575 (86.4)	1	1	1
Separated	404 (13.6)	0.949 (0.767; 1.174)	1.014 (0.804; 1.278)	0.990 (0.738; 1.327)
Siblings				
No	1162 (39.0)	1	1	1
Yes	1819 (61.0)	1.069 (0.921; 1.240)	1.026 (0.871; 1.208)	1.123 (0.912; 1.384)
Caregiver educational level				
Basic	1082 (36.3)	1	1	1
Secondary	900 (30.2)	0.862 (0.721; 1.031)	0.910 (0.748; 1.105)	0.970 (0.758; 1.240)
Higher	997 (33.5)	0.868 (0.730; 1.033)	0.864 (0.714; 1.046)	0.909 (0.714; 1.159)
Monthly household income (Euro)				
≤ 1000	741 (25.5)	1	1	1
1001 – 2000	1377 (47.2)	1.128 (0.942; 1.351)	1.006 (0.826; 1.225)	1.045 (0.813; 1.343)
2001 – 3000	581 (20.0)	1.047 (0.840; 1.305)	0.928 (0.729; 1.182)	0.961 (0.706; 1.310)
>3000 €	202 (7.0)	0.922 (0.671; 1.266)	0.945 (0.668; 1.336)	1.148 (0.753; 1.749)
Parental occupation				
Full-time	2129 (71.6)	1	1	1
Part-time	217 (17.3)	0.813 (0.610; 1.082)	0.711 (0.510; 0.991)	0.813 (0.533; 1.239)
Unpaid	629 (21.1)	0.925 (0.772; 1.107)	0.970 (0.796; 1.181)	1.055 (0.826; 1.347)
Concern about household expenses				
Never or rarely	180 (6.1)	1	1	1
Sometimes or a lot of times	658 (22.3)	0.764 (0.547; 1.065)	0.698 (0.488; 1.000)	0.751 (0.485; 1.163)
Almost always or always	2112 (71.6)	0.960 (0.707; 1.303)	0.867 (0.625; 1.201)	0.789 (0.530; 1.174)
Child's school type				
Private	311 (10.4)	1	1	1
Public	2657 (89.5)	1.051 (0.828; 1.334)	0.940 (0.727; 1.217)	1.049 (0.751; 1.466)
Social support				
Sports in a group or club				
No	2268 (76.4)	1	1	1
Yes	700 (23.6)	0.921 (0.776; 1.094)	0.995 (0.824; 1.200)	0.870 (0.681; 1.110)
Music activities				
No	2564 (86.1)	1	1	1
Yes	415 (13.9)	0.829 (0.671; 1.025)	0.830 (0.654; 1.052)	0.923 (0.686; 1.242)
Religious activities				
No	945 (31.7)	1	1	1
Yes	2032 (68.3)	0.891 (0.762; 1.041)	.737; 1.034)	.773; 1.190)
Psychosocial distress				
Behavior problems				
No	2607 (87.9)	1	1	1
Yes	360 (12.1)	0.984 (0.788; 1.230)	0.873 (0.680; 1.121)	1.092 (0.809; 1.473)
Socialization problems				
No	2778 (93.3)	1	1	1
Yes	198 (6.7)	1.046 (0.782; 1.399)	1.044 (0.760; 1.443)	0.787 (0.511; 1.214)

Figure 2. Associations (odds ratios and 95% confidence intervals) between indicators of living conditions and pediatric pain outcomes: any pain, multisite pain and pain of psychosocial (PS) onset (upper panel: girls, lower panel: boys).





Conclusions and implications for health education

With this thesis, we observed that gender shaping of the pain experience was already observable at age seven. Also, there was an interaction between parental and offspring genders which seemed to be a key influence on the reporting of pain, since mothers of girls reported higher frequency and worse severity than mothers of boys or fathers of children of both genders. However, there were important similarities in regard to pain of psychosocial onset, in both genders: family history of chronic pain was associated with the probability of reporting pain of psychosocial triggers. Moreover, regardless of the respondent, pain of psychosocial onset was associated with worse consequences in both genders, but more extensively among girls. This provides evidence that the psychosocial influence on the experience of pain starts early in life.

Specifically regarding chronic widespread pain features – multisite symptoms and psychosocial onset – we found that, at age seven, they were already present in both genders. Individual characteristics and classic socioeconomic markers, such as parental educational level and monthly household income, were not associated with the chronic widespread pain features studied. Only poor material living conditions were associated with the presence of multisite pain and pain of psychosocial onset. These findings suggest that, at this early age, classic measures of socioeconomic deprivation were not clear determinants of chronic widespread pain features at this life stage, even though living conditions might have specific relevance

The only way to successfully address a problem is to know it extensively. Pain is a complex problem which has been an object of numerous studies and prevention strategies; however, its incidence and burden remain high. There are still doubts about which will be the best age to act and what specific factors should be addressed first.

Well, this study provides some useful information in this field. Now we know that at age seven, where the influence of biological sexual development is still minimal, there is already an influence of gender roles on the perception and report of pain. Also, notably, psychosocial events are already associated with pain onset and with higher impact on children's daily lives. This being an age when children ingress school, their responsibilities increase and their social circle starts to extend, and knowing the importance given to psychosocial events, it would be interesting to address these issues in classes or group activities. Prevention strategies could be designed for this age group in order to start building more efficient coping strategies and to tackle some worries or fears.

Regarding chronic widespread pain risk, there is also useful information. Firstly, although early markers of this syndrome are already present in children aged seven, socioeconomic patterning

was not clear. This does not mean that this issue does not deserve attention at this age. Rather, it means that this might be a key timing for intervention before the syndrome becomes clinically manifest. An interesting finding regarding this subject was the association between living conditions and chronic widespread pain features. Since these conditions are in theory modifiable, they might be object of prevention and deserve attention. The links between poor housing conditions and poor health indicate that improving house conditions may be an important mechanism to lead to overall health improvement.

To sum up, this thesis adds knowledge regarding the circumstances in which pain emerges and manifests at such an early age. This provides useful information that can be used to plan and develop policies, prevention strategies and health education programs regarding pain experience early in the life course.

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